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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DEJONG, ERIC S	
ART UNIT	PAPER NUMBER
1631	
MAIL DATE	DELIVERY MODE
05/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,307	DAHIYAT ET AL.	
	Examiner	Art Unit	
	ERIC S. DEJONG	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2008 and 05 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicants supplemental response, filed 02/05/2008, to the Office action mailed 10/08/2007 is acknowledged.

Claims 6 is canceled. Claims 1-5 and 7-26 are pending and currently under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 101/112

The rejection of claims 1-5 and 7-26 rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility is withdrawn in view of amendments made to the instant claims.

The rejection of claims 1-5 and 7-26 are also rejected under 35 U.S.C. 112, first paragraph because one skilled in the art would not know how to use the claimed invention is withdrawn in view of amendments made to the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

It is further noted that the recent Supreme Court decision in KSR Intl. Co. v. Teleflex Inc. rejected the rigid approach of applying a strict TSM test as the sole basis for obviousness and that the analysis for obviousness need not seek out precise teachings directed to the specific subject matter of a claim. Further the decision set forth that the analysis can take into account the inferences and creative steps that a person of ordinary skill in the art could employ and that a person of ordinary skill in the art is also a person of ordinary creativity, not an automaton. Further, the decision set forth that a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

Claims 1-5 and 7-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hardman (IDS, filed 09/28/2004: US Patent No. 4,939,666) in view of Harayama (TIBTECH (1998)). This rejection is necessitated by amendments made to the instant claims.

The instant claims are drawn to a method for generating a secondary library of protein sequences with at least one desired characteristic relative to a target protein. The recited process comprises the steps of inputting coordinates of said target protein into a computer, selecting a plurality of positions from said target protein and applying a force field calculation thereto to generate a primary library, generating a probability distribution of amino acid residues in proteins of said primary library, combining a plurality of amino acids at primary variant positions within said target protein to generate a secondary library, and synthesizing and screening a plurality of the secondary variant protein sequences for the at least one desired activity.

Hardman sets forth a computer-assisted method of constructing a polypeptide chain having a substantially predetermined conformation wherein a stable well-mapped structure is used as a starting point and additional peptide units are incrementally added while maintaining favorable enthalpic and entropic contributions to stability (see Hardman, Abstract). The starting structure consists of a set of starting atomic positions in an XYZ coordinate space, and accommodates amino acid side chain atomic positions (see Hardman, Figure 1 and column 23, line 34 through column 24, line 34, and column 24, line 65 through column 25, line 33). Hardman further discloses procedures for

generating multiple alternative starting structures and storing such structures in a library (see Hardman, Column 26, line 54 through column 27, line 51). The steps of modifying various positions or groups of positions in the starting structure(s) and analyzing the subsequent modified structures using energetic considerations to generate a second set (a secondary library of variant protein sequences) is set forth Hardman in column 28, line 24 through column 33, line 57. Hardman further sets forth the protocols for producing the modeled proteins resulting from practicing the disclosed method as well as variants thereof (combining a plurality of protein variant sequences). See Hardman et al., column 42, line 7 through column 45, line 15.

Hardman further sets forth procedures for a merit selection step following the modification of starting structures that results in performing ranking and culling of candidates based on rule-based expert decisions and numerical calculation of figures of merit (see Hardman, column 33, line 56 through column 33, line 32). Further, Hardman discloses a figure-of-merit estimation procedure that is implemented to provide a general functionality description for the resultant structures and reads on generating a probability distribution. (see Hardman, column 35, line 56 through column 36, line 6). Hardman teaches that enzymes are one of several types of proteins suitable for use in the disclosed methodology. See Hardman, column 4, lines 3-10. Hardman teaches that the disclosed methodology is particularly advantages for the design of proteins as drugs. See Hardman, column 21, lines 26-42. Hardman sets forth the above described methods for constructing polypeptide chains having a substantially predetermined conformation wherein a stable well-mapped structure is used as a starting point, and

additional peptide units are incrementally added while maintaining favorable enthalpic and entropic contributions to stability.

Hardman et al. does not expressly disclose the synthesis and screening of the polypeptides designed by the above described method. However, Hardman does teach that once structures have been designed and demonstrated to have at least partial functionality, mutagentic methods can be used to induce random in the protein product being expressed (see Hardman et al., col. 45, lines 16-27).

Harayama sets forth the application of improving enzymes and proteins by DNA shuffling that involved subjecting segments of an assembly to random mutagenesis by error-prone PCR. The applied methodology is taught to provide new procedures to obtain improved enzymes in combination with established methods of rational protein design (see Harayama, Abstract and page 76, line 1 through page 77, line 35). Harayama additionally teaches a practical strategy for altering enzyme properties is to introduce random base substitution and then select or screen for desired variants. A critical point of this strategy is the mutation frequencies introduced need to be carefully tuned as the combination of beneficial mutations a deleterious mutation may result in the formation of an inactive enzyme (see Harayama, page 78, column 2, lines 30-59).

Therefore it would have been obvious to one of skill in the art employ the disclosed methods of producing variant proteins, DNA shuffling, and error-prone PCR, as taught by Harayama, in combination with the methods of rational protein design, as taught by Hardman, because Hardman et al. suggests the use of mutagenesis procedures to improve upon designed polypeptides and, further, Harayama expressly

teaches that the disclosed shuffling improves rational protein design. One of ordinary skill in the art would further recognize that applying the known techniques producing variant proteins, as taught by Harayama, in combination with variant sequences generated by known protein design methods, as taught by Hardman, would yield only predictable results.

Response to Arguments

Applicant's arguments filed 02/05/2008 have been considered but are moot in view of the new grounds of rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Moran Marjorie can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric S DeJong
Primary Examiner
Art Unit 1631

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